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Determining the Phospholipid Packing within a Lipoprotein Particle Using Diffuse Scattering from Crystals and SAXS C. Peters-Libeu, Y. Newhouse and K. Weisgraber J. David Gladstone Inst. of Neurological Disease, 1650 Owens St., San Francisco, CA USA 94158.

Human apolipoprotein E•DPPC dipalmitoylphosphatidylcholine (DPPC) particles mimic apoE-containing high density lipoprotein particles found in the brain and plasma. These high density lipoproteins play an active role in cholesterol transport through binding between apoE and members of the LDL-receptor family. Although the apoE•DPPC particles crystallize readily and diffract anisotropically to 7-12Å, the diffraction patterns are a composite of Bragg scattering from the ordered protein atoms and diffuse scattering from the partially ordered phospholipid. Analysis of the diffuse scattering reveals the shape of the apoE•DPPC particle, defines the orientation of the lipids with respect to the molecular envelope of the protein and defines average packing parameters for the phospholipid hydrocarbon tails. SAXS was used to confirm the shape of the apoE•DPPC particle in solution. Using this information, we have generated a model of apoE•DPPC particles in which the overall shape of the particle is spheroidal in contrast to the prevailing assumption that these particles would be discoidal. In addition, we modeled the conformational change which occurs in the LDL-receptor binding region of apoE when it binds to DPPC.